REMARKS

Claims 14, 17, 19-20, 23-24, 26-27, 29 and 31 remain under active prosecution in the present application.

By way of review, the present invention provides a quick and effective method for assessing in a patient whether there has been axonal damage resulting from a traumatic CNS injury, and the extent of that damage. Until now, there has been no effective, minimally invasive procedure for quickly determining that information which, of course, can be critical in an emergency room setting. In this method, a patient suspected of having such traumatic CNS injury, such as a head trauma, provides a sample of cerebrospinal fluid. The presence in that fluid of specific tau proteins are then determined using a monoclonal antibody raised against those proteins, and the levels of those proteins in the fluid are compared to control samples representing both damaged and undamaged states. This comparison yields information regarding whether there has been a traumatic CNS injury and the extent of that injury in the patient.

The objections raised by the Examiner in the Office Action will now be considered sequentially, referring to the paragraph numbers used by the Examiner in the Office Action.

Paragraph 9. The Examiner has rejected the claims, under the first paragraph of 35 U.S.C. § 112, based on the use of the phrase "fragments thereof" with respect to generalized fragments of the protein of SEQ ID NO:1. In order to address that objection, the generalized language regarding fragments has been eliminated from claim 14. That language does not appear in claim 31, the other independent claim under consideration. In light of this amendment, it is respectfully submitted that this rejection has been overcome and it is requested that it be withdrawn.

Paragraph 10. The Examiner has rejected the claims of the present application, under the second paragraph of 35 U.S.C. § 112, based on certain language utilized in the claims. In response to those rejections, the language of claim 15 has been incorporated into independent claims 14 and 31 herein. In light of this amendment, claim 15 has been canceled as being redundant. All claims of the present application now require that the amount of protein measured in the assay defined in the present application be compared to control samples.

Further, in response to the Examiner's comments, claims 14 and 31 have been amended to delete the Markush language used therein. In light of these amendments, it is submitted that the rejection under the second paragraph of 35 U.S.C. § 112 has been overcome and it is respectfully requested that it be withdrawn.

Paragraph 11. The Examiner has rejected claims 17 and 24 based on their use of the language "less that 50 kDa". In response to this rejection, claims 17 and 24 have been amended so as to eliminate the language objected to by the Examiner and replace it with a range of from about 30 to about 50 kDa. In light of these amendments, claims 18 and 25 have been canceled as being redundant. These amendments overcome the rejections of the claims made by the Examiner in paragraph 11, and it is therefore respectfully requested that those rejections be withdrawn.

Paragraph 12. The Examiner has rejected claim 30, under the second paragraph of 35 U.S.C. § 112, for being indefinite in the use of the phrase "a patient with a neurological disease". Claim 30 has been canceled herein, thereby rendering this objection moot. Accordingly, it is respectfully requested that it be withdrawn.

Paragraph 13. Finally, the Examiner has rejected claims 14-15, 17-20, 23-27 and 29-31, under 35 U.S.C. § 102(b), as being anticipated by Vandermeeren et al. (WO94/13795). The primary reason for this rejection is that Vandermeeren teaches the use of an assay for Alzheimer's Disease and the claims pending in the present application, prior to this amendment, encompassed Alzheimer's Disease. Claims 14 and 31, the independent claims of the present application, have been amended herein so as to clearly define that the assay covered by those claims is to detect the presence and extent of traumatic central nervous system injury, such as head trauma, and not for the purpose of detecting the presence or extent of degenerative diseases, such as Alzheimer's Disease. The Vandermeeren reference does not in any way suggest the use of its assay for the detection of traumatic CNS injury. Alzheimer's Disease would clearly not be considered a traumatic CNS injury since it occurs slowly over time and not as the result of a trauma event (i.e., it is degenerative). Accordingly, since the Vandermeeren patent neither discloses nor suggests the use of a tau protein assay to detect the presence or the extent of traumatic CNS injury, the claims of the present application, as amended herein, are patentable over the Vandermeeren patent. In light of this,

the rejection based on Vandermeeren is improper and it is respectfully requested that it be withdrawn.

In light of the amendments and remarks made herein, it is respectfully submitted that the claims currently pending in the present application are now in form for allowance. Accordingly, reconsideration and allowance of those claims, as amended herein, are earnestly solicited.

Respectfully submitted,

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CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to Box Non-Fee Amendment, The Assistant Commissioner for Patents, Washington, D.C., 20231, this 17th day of October, 2001.

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Appendix A
Marked Version Showing Changes Made

Claims 14, 17 and 31 are amended as follows:

Claim 14 (three times amended), A method of determining axonal damage in the central nervous system of a patient suspected of having a [condition selected from primary neuronal injuries, primary hemorrhages, primary vascular injuries, dural sinus laceration or occlusion, traumatic pia-arachnoid injuries, cranial nerve injuries, and secondary traumatic lesions] traumatic central nervous system injury, said method comprising the steps:

(a) obtaining a sample of cerebrospinal fluid from said patient;

(b) treating said sample of cerebrospinal fluid with at least one monoclonal antibody, said at least one monoclonal antibody having been raised against an axonally-derived protein [selected from the group consisting] in the form of an isoform[s] of tau protein of SEQ ID NO:1 [and fragments thereof]; [and]

(c) detecting the presence of said axonally-derived protein bound to said at least one monoclonal antibody[.]; and

(d) comparing the amount of said axonally-derived protein bound to said at least one monoclonal antibody in step (c) to control samples from the group representing a normal undamaged axon state and those representing an axonal damage state.

Claim 17 (three times amended). A method according to Claim 14 wherein said axonally-derived protein is a fragment of said tau protein of SEQ ID NO:1 demonstrating an apparent molecular weight [less than] in the range of about 30 kDa to about 50 kDa.

Claim 24 (three times amended). A method according to Claim 23 wherein said axonally-derived protein bound to said at least one monoclonal antibody is a fragment of tau protein SEQ ID NO:1 which is detected through gel electrophoresis and which gives rise to an electrophoresis gel demonstrating multiple protein bonds with apparent molecular weights [less than] from about 30 kDa to about 50 kDa.

Claim 31 (amended). A method of determining axonal damage in the central nervous system of a patient suspected of having [a condition selected from primary neuronal injuries, primary hemorrhages, primary vascular injuries, dural sinus laceration or occlusion, traumatic pia-arachnoid injuries, cranial nerve injuries, and secondary traumatic lesions] traumatic central nervous system injury, said method comprising the steps of:

(a) obtaining a sample of cerebrospinal fluid from said patient;

(b) treating said sample of cerebrospinal fluid with at least one monoclonal antibody, said at least one monoclonal antibody having been raised against an axonally-derived protein [selected from the group consisting of] in the form of an isoform[s] of tau protein of SEQ ID NO:1; [and]

(c) detecting the presence of said axonally-derived protein bound to said at least one monoclonal antibody; and

(d) comparing the amount of said axonally-derived protein bound to said at least one monoclonal antibody in step (c) to control samples selected from the group representing a normal undamaged axon state and those representing an axonal damage state.

Claims 15, 18, 25 and 30 are canceled.